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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 4, 7-9 and 11 are rejected under 35 U.S.C. §103(a) as being unpatentable over Ho *et al.* (WO 01/54701) in view of Kent *et al.* (WO 00/28003, cited in IDS filed 26 October 2006).

The instant claims are directed to a method comprising administering to a subject a poxvirus vector encoding an HIV antigen and IFN-γ, in conjunction with interrupted anti-retroviral drug therapy.

Ho *et al.* teaches a method of permitting cessation of antiviral therapy on HIV-infected subjects, who have a viral load of less than 5,000 viral copies per ml of plasma (limitation in claims 3 and 4) and a $CD4^+$ T-cell count of above 500 cells/ml, and who have been treated with a potent combination of antiviral agents that contributed to a lower viral copy number and equal or higher $CD4^+$ T-cell count than before treatment, without virus rebound or with at least a delayed virus rebound or a decreased post-rebound viral load, by inducing both humoral and cell-mediated immunity and achieving

an immunological control of persistent infectious virus after discontinuation of antiviral therapy (page 2, lines 15-34). The method comprises inducing HIV-specific (limitation in claim 2) immune responses by administering an attenuated recombinant poxvirus (e.g., avipox, vaccinia virus, or recombinants thereof) that includes [one] or more nucleic acids encoding one or more HIV-specific immunogens (page 3, lines 2-5, page 9, lines 12-22 and claim 21).

Although Ho *et al.* specifically suggests combining an HIV antigen with an immunostimulatory or co-stimulatory molecules such as interleukin 2, which is a cytokine (page 3, lines 6-9), Ho *et al.* does not disclose co-expressing IFN-γ with an HIV antigen in the poxvirus vector.

Kent *et al.* discloses an immunogenic construct comprising an avipox virus vector encoding HIV-1 Gag and/or Pol or derivatives thereof and interferon-gamma (IFN-γ) or a functional derivative thereof that is effective in inducing, enhancing or otherwise stimulating an immune response to HIV Gag and/or Pol. See page 3, lines 15-31.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Ho *et al.* so as to replace the poxvirus vector with the avipox vector taught by Ho et al. encoding HIV-1 Gag and/or Pol or derivatives thereof and IFN-γ or a functional derivative thereof as taught by Kent *et al.* or to include IFN-γ in the vector of Ho et al. One having ordinary skill in the art would have been motivated to make such a modification to enhance the HIV-specific immune responses by additionally expressing IFN-γ as taught by Kent *et al.* (see, for example, page 28, lines 4-14). There would have been a reasonable expectation of success,

given the effectiveness of the avipox vector encoding HIV-1 Gag and/or Pol and IFN-γ in inducing, enhancing or otherwise stimulating an immune response to HIV Gag and/or Pol, as taught by Kent *et al*.

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

In the reply dated September 8, 2010, applicant first argues that the combined teachings are not adequate. Specifically, applicant argues that of four patients who discontinued therapy "only two of four patients exhibited a delayed rebound in plasma viremia." Applicant's assessment is correct. However, applicant is reminded that Ho et al. is not required to demonstrated 100% success with all vaccination trials.

Applicant next argues that a single reference (Markowitz et al.) "casts doubt" on the observations made by Ho et al. Applicant's arguments and the cited reference have been fully considered but not found persuasive. Markowitz et al. does not cite or mention Ho et al. nor does it "cast doubt" on the data and observations present in Ho et al., which clearly demonstrated a delayed rebound after discontinuation of therapy. There can be a number of reasons Markowitz et al. obtained the results discussed reported in the reference. It is possible that Markowitz et al. performed a different experiment from Ho et al. Regardless, the Office does not have the resources to determine why or how Markowitz et al. obtained its results.

Applicant next argues that there is a lack of motivation to combine Ho et al. and Kent et al. This argument too has been fully considered but not found persuasive.

As outlined above, Ho et al. teaches a method comprises inducing HIV-specific (limitation in claim 2) immune responses by administering an attenuated recombinant poxvirus (e.g., avipox, vaccinia virus, or recombinants thereof) that includes [one] or more nucleic acids encoding one or more HIV-specific immunogens (page 3, lines 2-5, page 9, lines 12-22 and claim 21). Ho et al. further teaches that the vaccine can be combined with an immunostimulatory or co-stimulatory molecules such as interleukin 2, in an amount that is sufficient to potentiate T-cell responses, in particular CD8+ responses. It is well known in the art that IFN-γ potentiates TH1 and CD8+ responses by inhibiting viral replication, activating macrophages and recruiting them to the site of infection, and increasing the expression of peptide-bound MHC class I molecules. In addition, it is well known that TNF-β potentiates CD8+ responses by synergizing with IFN-γ in killing target cells. Thus, even without the teachings of Kent et al. one of ordinary skill in the art using the teachings of Ho et al. would know that IFN-γ can be combined with the vaccine taught by Ho et al. However, when considering the teachings of Kent et al., which discloses an immunogenic construct comprising an avipox virus vector encoding HIV-1 proteins and interferon-gamma (IFN-γ) that is effective in inducing, enhancing or otherwise stimulating an immune response to HIV Gag and/or Pol, it would have been obvious to one of ordinary skill in the art to modify the method of Ho *et al.* so as to include IFN-γ as suggested by Ho et al. and as taught by Kent *et al.* One would have been motivated to make such a modification to potentiate CD8+ responses and to enhance the HIV-specific immune responses as suggested by Ho et al. and as taught by Kent *et al.*

Applicant next argues that Ho et al. does not comment on why two of four patients did not exhibit a delayed rebound. Again, applicants are reminded that Ho et al. is not required to demonstrated 100% success with the claimed method. Applicants also cite Rosenwirth and Markowitz et al. to establish failed attempts in the art to reduce or delay viral rebound. It is not clear why applicant cited these references. Failures in the art do not diminish or negate the results of Ho et al.

Applicant next argues that there is no reasonable expectation of success because the protocol of Ho et al. is extremely complex, because Ho et al. stated that the vaccines being used were novel, and because of the failures in the art. Applicant also argues that Ho et al. administered proteins as opposed to nucleic acids in the vaccine trial. The Office does not have sufficient information to comment on the complexity of the protocol of Ho et al. However, the Office can comment that the protocol demonstrated a delayed rebound in plasma viremia. With regard to nucleic acids vaccines, Ho et al. teaches the use of nucleic acid vaccines (see, for example, pages 8 and 11)

Applicant finally argues that applicant was the first to disclose an avipox vector encoding an HIV antigen and interferon-γ suitable for administration to an HIV-infected subject in the absence of anti-retroviral drug treatment; and, secondly, such administration resulted in a reduction or delay of viral rebound during interruption of anti-retroviral drug treatment, in the absence of a detectable immunological response to HIV. This argument has been addressed above.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NICOLE KINSEY WHITE whose telephone number is (571)272-9943. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zacharia Lucas can be reached on (571) 272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nicole Kinsey White/
Examiner, Art Unit 1648

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